

Prophylactic Immunization and Poliomyelitis

MARY WALTON, Sr. Surgeon*

Early in the epidemic of poliomyelitis which began in the state of Victoria, Australia, in January 1949, attention was directed toward a possible relationship between prophylactic inoculations and paralytic poliomyelitis. Sporadic cases of paralysis following the injection of an antigen had been reported in England during the progress of the immunization campaign which began in 1942, but there was no evidence to suggest a causal relationship. A few cases early in the Victoria epidemic who had received injections of single or combined antigens shortly before onset of their disease led Dr. B. P. McCloskey, Poliomyelitis Officer of the State Health Department, Melbourne, Australia, to include a history of immunization as a part of the routine investigation of reported cases (1). This information was obtained from the parents of 340 of the 375 cases reported between January and August. McCloskey determined the sites and severity of paralysis and checked the dates and sites of injections of the 35 cases where any inoculation had been reported within 3 months of onset of poliomyelitis. He presented evidence to show that, in the Victoria epidemic, in 31 cases known to have received an injection of diphtheria toxoid or pertussis vaccine, alone or in combination, within 3 months of their onset, paralysis was more frequent in the inoculated than in the uninoculated limbs. Twenty-six out of 35 inoculated limbs were paralyzed. Of the 89 uninoculated limbs, 17 were paralyzed. In addition, of the 16 cases under 3 years of age receiving inoculation within 35 days of onset of illness and for which complete data were available, paralysis occurred in the limb last inoculated before onset in 15; and there was a considerable increase in the severity of the paralysis in the last inoculated limb as compared with the degree of paralysis in each limb of a control group of children.

In London, Dr. J. K. Martin from the Department of Child Health, Guy's and Evalina Hospitals, reported 17 observed cases occurring between 1944 and 1949, in which paralysis was preceded by

injection within 28 days of onset, and 78 additional cases occurring between 1941 and 1949, for which records were available for study (2).

Dr. D. H. Geffen, Medical Officer of Health, Metropolitan Borough of St. Pancras, London, investigated all cases of poliomyelitis reported in the borough in the 1949 epidemic and found six who had contracted polio within 22 days of immunization. He then obtained further information from other boroughs in London and presented data on site of injection and site of paralysis of a total of 29 cases in children under 5 years of age where inoculation within 28 days was associated with paralysis of the injected limb (3).

On the basis of the above reports it appeared unlikely that the association between inoculation and paralysis was by chance, and a statistical study was undertaken by Hill and Knowelden of the Department of Medical Statistics, London School of Hygiene and Tropical Medicine (4). Since the need for a rapid answer made it impractical to follow a sufficient number of immunized children of given ages to observe the risk of development of poliomyelitis, another approach was used in this study. Records were obtained from 33 widespread areas in England of relatively high incidence of polio during July, August, and September of 1949. Local health officers were requested to obtain from reported polio cases under 5 years of age such data as sex, birth date, paralysis, and inoculation history. A control group was sought among children of similar sex and age who were reported as having measles at about the same time but after the onset date of their paired polio cases. Since there were insufficient numbers of measles cases reported, approximately half of the controls were made up by selecting from the local birth registers another child whose birth date was as close as possible to that of the paralytic polio case who was of the same sex, and still in the same area so that information on inoculation could be obtained. One hundred sixty-four controls that could be paired with cases were secured. On the question of site of paralysis and previous inoculation, data obtained in this study indicated that there was no evidence that an injection 3 or

*Epidemiologic Services, CDC

more months previous to the illness affected the distribution of paralysis in any way. Thirty-five children under 2 years of age and seven children between 2 and 5 years of age were found who had had an inoculation less than 1 month before the onset of paralytic disease. In the group of inoculated children under 2 years of age, the legs were proportionately less affected than in uninoculated children and there was a striking preference for the left arm, which is the usual site of inoculation. Twenty-nine of thirty-six, or 81 percent, of the children under 2 years of age had paralysis in the limb of injection although not necessarily confined to that limb. This proportion is greatly in excess of the figure (13 of 65 or 20 percent) shown by children whose last injection was more than 1 month before onset. In comparing the inoculation histories of the children with poliomyelitis with the histories of their controls in the 164 pairs for which a satisfactory control could be found, there is a striking difference in the frequency of the history of immunization less than 1 month before the onset of the poliomyelitis case. Sixteen of the 164 polio cases gave such a history while only one of the controls had had an inoculation within a month of the onset of its paired polio case. At other intervals there is no difference between the polio cases and their controls in history of inoculation. With respect to the time interval between inoculation and onset of poliomyelitis, 26 of the 33 children who had paralysis within 28 days in the limb of injection showed an interval of 8 to 17 days. None fell below 8 days.

These studies would seem to indicate that the distribution of sites of paralysis are abnormal in children who have been inoculated within a month preceding the onset of their illness. In recently inoculated children the limb of injection is a site of paralysis much more frequently than is the case in children not recently inoculated. The difference in history of immunization within a month of onset in the pairs of polio cases and their controls indicates that some of the cases in the polio group may have been precipitated by the inoculation.

In order to investigate the question as to whether a similar situation exists in the United States, Dr. Gaylord Anderson, University of Minnesota, reviewed case histories of 2,709 cases of polio which occurred during the 1946 outbreak in Minnesota (5). Among the items included in the case histories taken in 1946 was a question about all injections or immunizations the patients had

ever received, the date, and the name of the physician. A total of 2,677 contained a definite record of immunization or a specific statement that the patient had never been immunized. All histories of children 7 years of age or under were selected for more detailed study of the relationship to prior immunization. In 85 cases, confirmation was obtained from physician or clinic of a definite record of immunization during the 6 months prior to the attack of poliomyelitis. Of the 85, 33 were cases in which onset of polio occurred within 1 month after the most recent injection, 12 in the second succeeding month, and 16 in the third, indicating a concentration of cases occurring within a month following injection. Of the total of 33 cases with confirmed history of immunization within the month preceding onset of polio, 19 cases, or 58 percent showed a correlated paralysis, that is, paralysis of the limb which was the site of the injection, while of 52 cases occurring 2 to 6 months subsequent to antigen injection, only 8 cases, or 15 percent, were correlated. Also 20 cases, or 61 percent of the 33 immunized during the preceding month had arm involvement, as contrasted with only 11 cases, or 21 percent, of 52 which were immunized 2 to 6 months preceding, 19 percent of the sample immunized before 1946, and 21 percent of those who had never been immunized. In addition to the apparent concentration of cases during the first month after immunization and a tendency toward localization of the paralysis in the limb into which the injection had been given, 24 cases, or 73 percent, of the 33 first month cases were classed as severe spinal cases, as contrasted with 42 percent of the 2- to 6-month group. This, however, may be related to a difference in age distribution, since the patients in the 1-month group were younger. To correct for this, members of the group under 2 years were compared, and although these figures are very small there is a definite suggestion that the first month cases were more severe. Analysis of the time interval between last antigen injection and onset of illness lends further support to the idea of a causal relationship. Of the 33 cases, 17 developed in the 10- to 14-day interval and 20 in 5 to 14 days. Eleven of the 19 correlated cases developed in the 10- to 14-day interval and 16 of the 19 in the 5- to 19-day interval, while the interval of noncorrelated cases showed less concentration. To shed further light on the duration of this possible effect, all the case histories obtained during the outbreak were reviewed from the point of view of history of various types of immunization

and types of response to polio infection. No differences were noted. Whatever effect the antigens may have had in conditioning paralysis during the first month following injection, apparently it was not permanent.

To obtain further information on this question, a study was set up by the New York State Department of Health during the summer of 1950. A total of 2,137 cases of polio was studied and for each a history was obtained regarding all injections received during the 2 months prior to onset of disease. Control information identical with that from the cases was obtained from 6,055 case household members and from a group of 14,710 persons made up of the household members of three additional control families for each case family. Analysis of these data showed that the history of an injection during the month before onset was twice as frequent among polio patients as among the controls. This ratio was about the same for immunizing agents, penicillin, and a miscellaneous group of other injections. The analysis also disclosed that the risk of getting paralytic polio at each age group is doubled in the recently injected population. In addition, clear-cut association was demonstrated between site of injection and site of paralysis.

The evidence seems conclusive that the location of the paralysis produced by the virus of poliomyelitis may be conditioned in some cases by recent injections. The recent study in New York State indicates that antigen injections apparently are no different from injections of other miscellaneous materials. There has been suspicion, which the New York study would seem to confirm, that injections may be a factor in determining the difference between a recognizable paralytic infection and an unrecognized or nonparalytic involvement. All of the data indicate that the effect is transient, its influence appearing not to persist for longer than 1 month. Although the risk of increasing the susceptibility to poliomyelitis by the injection of immunizing agents or other material is slight, it should be taken into consideration when elective injections are given. Immunization procedures for the prevention and control of acute communicable diseases need not and should not be curtailed. Since the effect of an injection on susceptibility to paralytic poliomyelitis does not appear to persist longer than 1 month, routine prophylactic inoculations can be easily carried

out at times when the prevalence of poliomyelitis virus is not likely to be high.

A report of an *ad hoc* subcommittee of the Committee on Research and Standards of the American Public Health Association, accepted by this Committee, states as follows (7):

"Recent published and unpublished data strongly suggest that an individual who develops poliomyelitis within a month after receipt of injection of an antigen, or possibly of some other material, shows an increased frequency of paralysis in the extremity into which the injection has been given. There are also suggestions that among the reported cases of poliomyelitis are cases 'which would not have been clinically diagnosed as poliomyelitis at all if their (recent) inoculation had not brought them into the paralytic group.'

"Although further studies on these questions are imperative, the data so far available would suggest that, in the face of an abnormal prevalence of poliomyelitis in a given locality, antigen inoculations may well be postponed until after the subsidence of the abnormal prevalence. It should be stressed, however, that there is no evidence that this effect of inoculation persists for more than one month. On the contrary, the risk of poliomyelitis among persons who have been immunized more than one month before onset is no greater than among non-immunized persons."

REFERENCES

1. McCloskey, Bertram P.: The relation of prophylactic inoculations to the onset of poliomyelitis. *Lancet* 1:659-663 (1950).
2. Martin, J. K.: Local paralysis in children after injections. *Arch. Dis. Childhood* 50:1-14 (1950).
3. Geffen, Dennis H.: The incidence of paralysis occurring in London children within four weeks after immunization. *Med. Off.* 83:137-140 (1950).
4. Hill, A. Bradford and Knowelden, J.: Inoculation and poliomyelitis. *Brit. M. J.* 2:1-6 (1950).
5. Anderson, Gaylord W. and Skaar, A. E.: Poliomyelitis occurring after antigen injections. *Pediatrics* July 1951 (to be published).
6. Korns, R. F., Albrecht, R. M., Locke, F.: Parenteral injections with paralysis in poliomyelitis. (to be presented at APHA).
7. Polio and immunizations. *Am. J. Pub. Health* 41(6):746-747 (1951).